REMARKS

Claims 1-23 were pending in this application. By this Amendment claims 2-4, 20 and 22-23 have been canceled, and claims 1, 5, 9 and 21 have been amended. Upon entry, claims 1, 5-19 and 21 are now pending and under examination.

The Specification has been amended to correctly present the trademark SANDOSTATIN LAR® and its generic terminology.

Support for the amendment of claim 1 may be found, *inter alia*, in original claims 2-4 and 20. Claims 5 and 21 have been amended to change their dependency from canceled claims to a pending claim. Claim 9 has been amended to correct an incidence of lack of antecedent basis. Applicants maintain that the amendments do not raise an issue of new matter. Entry of the amendments is respectfully requested.

CLAIMS NOT INDEFINITE

Claims 1-23 have been rejected under 35 USC 112, second paragraph, as allegedly being indefinite. The rejection is respectfully traversed.

The Office Action pointed out certain informalities in claims 1, 9, 22 and 23. Claims 22-23 have been canceled. Claims 1 and 9 have been amended to address the defects pointed out in the rejection. Accordingly, applicants submit that the Section 112, second paragraph, rejection has been overcome.

CLAIMS ARE ENABLED

Claims 1-4, 6, 7 and 16-23 have been rejected under 35 USC 112, first paragraph, as allegedly not being enabled by the specification. This rejection is respectfully traversed.

The rejection has taken the position that the specification is enabling for treating a carcinoid tumor with the mesogenic strain MK107 of Newcastle Disease Virus, but not for any negative-stranded RNA virus, any replication-competent oncolytic virus, any Paramyxovirus, any strain of NDV or any mesogenic strain of NDV, other than MK07.

The rejection cites Sinkovics and Horvath (2000) for the proposition that at the time the invention was made only certain NDV strains were "labeled" as antineoplastic agents for human tumors. The rejection also quotes the statement in Sinkovics and Horvath that, "[v]arious NDV strains differ widely in their biological effects including oncolysis and without specific studies of a given NDV strain, generalizations that it is oncolytic just because it is a NDV strain are invalid and unacceptable." (Sinkovics and Horvath (2000) page 11.) On the other hand, applicants claimed that NDV generally would be useful in the claimed method. Who was right? The scientific literature supports applicants' position.

The rejection has taken the position that only a subset of NDV strains are oncolytic and that undue experimentation would have been required to identify them. The rejections stated, "It appears that . . . essentially all of the work required to identify other viruses as listed above has been left for others." (Office Action, page 6). If true one would have expected testing of a variety of NDV strains to yield frequent negative results. But the actual experience of researchers in the field is to the contrary.

Krishnamurthy, et al. infected a number of tumor and normal cell lines with five different NDV cell lines, Beaudette C, Kansas, California, La Sota, and Australian-Victoria, at a low multiplicity of infection (MOI = 0.001). "[A]ll of the NDV strains tested . . . selectively replicate and grow in tumor cells." (Krishnamurthy, et al., "Differentially Regulated Interferon Response Determines the Outcome of Newcastle Disease Virus Infection in Normal and Tumor Cell Lines" J. Virol. (2006) 80(11): 5145-5155 at 5153, end of last full paragraph. See results on pp. 5147-5148.) (copy enclosed with the IDS submitted concurrently herewith). The 100% success rate reported by Krishnamurthy is inconsistent with the rejection's assertion that undue experimentation would have been required to identify oncolytic strains of NDV from non-

oncolytic strains. Rather, for Krishnamurthy at least, identifying oncolytic strains of NDV was more like shooting fish in a barrel.

Neither the Sinkovics and Horvath reference nor the Wildner reference report negative results with any NDV strain that was actually tested. Nor has the Office pointed to any experimental evidence supporting its contention that NDV strains generally are not oncolytic.

Neither Sinkovics and Horvath (2000) nor Wilder (2001) address the mechanism for NDV's tumor selectivity. If the mechanism for tumor selectivity is broadly applicable across NDV strains, then one can conclude that NDV generally has antineoplstic properties. When Horvath, one of the authors of Sinkovics and Horvath (2000), later discussed NDV in cancer treatment and the mechanism of NDV's tumor selectivity he referred to the mechanism broadly as a property of NDV and not as limited to specific strains. (Horvath, "Newcastle Diseaes Virus: Its Oncolytic Properties" in Viral Therapy of Human Cancers, Sinkovics and Horvath eds., (Marcel Dekker, New York 2005) Chapter 5, pp. 533-574 at 539-547). One of the applicants and his colleagues had earlier discovered that tumor-specific defects in the antiviral response allow for NDV-specific replication in tumor cells compared to normal cells (See WO 00/62735, pages 11-15) (already of record). Accordingly the positive results demonstrated in the instant application utilizing one NDV strain are generalizable to NDV generally, and would have been understood as such by those of skill in the art who knew about the mechanism of NDV's tumor selectivity.

Applicants respectfully submit that the enablement rejection has been overcome and should be withdrawn.

CLAIMED INVENTION IS NOVEL

Claims 1-20 have been rejected under 35 USC 102(b) as allegedly being anticipated by Roberts et al. (WO 00/62735) as evidenced by Chandler et al., Martensson et al., Drougas et al. and Wessels et al. This rejection is respectfully traversed.

Claim 1 is directed to a method for treating a mammalian subject having a carcinoid tumor and carcinoid syndrome, comprising administering to the subject an amount of a therapeutic virus effective to treat the tumor and decrease one or more symptoms of the carcinoid syndrome, wherein the virus is a replication-competent Newcastle Disease virus. The rejection acknowledges that Roberts does not expressly teach treating carcinoid syndrome, but has taken the position that the reduction or treatment of carcinoid syndrome using Newcastle Disease virus (NDV) is inherent in the teaching of Roberts. The rejection stated:

> . . . it is well known in the art that **carcinoid tumors cause carcinoid syndrome**. It is also well known that treating or reducing the size of the tumor . . . results in a decrease or elimination of carcinoid syndrome. . . . Therefore . . . treating carcinoid tumors with . . . NDV . . . to reduce the size of or eliminate the tumors will **inherently** reduce or treat carcinoid syndrome. . . . (October 10, 2006 Office Action, page 10) (emphasis added).

This rejection on grounds of alleged inherent anticipation might be well taken if carcinoid tumors always caused carcinoid syndrome. But carcinoid tumors do not always cause carcinoid syndrome. According to McCormick, "Less than 10% of patients with carcinoids develop this syndrome." (McCormick, "Carcinoid Tumors and Syndrome," Gastroenterology Nursing (2001) 25(3):105-111 at 108, left column, third full paragraph) (copy enclosed with the IDS submitted concurrently herewith).

Because carcinoid syndrome is found in only a subset of carcinoid tumor patients, the treatment of carcinoid syndrome is not inherent in the teaching of Roberts. It is well established that "[i]nherency . . . may not be established by probabilities or possibilities." (Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1269, 20 USPQ2d 1746, ____ (Fed. Cir. 1991), quoting In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981)). Accordingly the rejection over Roberts for alleged anticipation is improper and should be withdrawn.

Claims 1-8, 13, 14 and 16-18 have been rejected under 35 USC 102(a) as allegedly being anticipated by Pecora et al. as evidenced by Laurie et al. Claims 1-8, 17 and 18 have been rejected under 35 USC 102(b) as allegedly being anticipated by Lorence et al. (WO 94/25627).

Claims 1-4, 6, 17 and 18 have been rejected under 35 USC 102(b) as allegedly being anticipated by Phuangsab et al. Claims 1-4, 17 and 18 have been rejected under 35 USC 102(b) as allegedly being anticipated by Reichard et al. Claims 1-8, 17 and 18 have been rejected under 35 USC 102(e) as allegedly being anticipated by Lorence et al. (US Patent No. 7,056,689). These rejections are respectfully traversed. Claim 1, which is the sole independent claim, has been amended to incorporate the limitations of original claim 20, which the Office has found to be novel over each of the foregoing references. Accordingly applicants submit that these rejections have been overcome.

Claims 22 and 23 have been rejected under 35 USC 102(a) as allegedly being anticipated by 9th Annual Ottawa Life Science International Conference and Exhibition (November 4-6, 2002). This rejection is respectfully traversed. In view of the cancellation of claims 22-23 this rejection is moot and should be withdrawn.

CLAIMED INVENTION IS NONOBVIOUS

Claims 9 and 10 have been rejected under 35 USC 103(a) as allegedly being unpatentable over Pecora, et al. This rejection is respectfully traversed. Claim 1, from which claims 9 and 10 depend, has been amended to incorporate the limitations of original claim 20. The Office has found claim 20 to be patentable over Pecora, et al. Accordingly applicants respectfully submit that the obviousness rejection has been overcome.

NO DOUBLE PATENTING

Claims 1-8 and 16-17 have been rejected for alleged obviousness-type double patenting over claims 1-3, 6, 7, 19, 22-25 and 27 of U.S. Patent No. 7,056,689. Claims 13-15 have been provisionally rejected for alleged obviousness-type double patenting over claims 157-161, 163-170, 172, 174, 183, 196-219 and 230-232 of copending Application No. 09/958,809. Claims 1-8, 13, 16 and 17 have been provisionally rejected for alleged obviousness-type double patenting over claims 1-3, 6-8, 50, 51, 63-65, 69, 70, 73, 115-120, 132, 134, 136 and 144 of copending

Application No. 10/167,652. Claims 13-15 have been provisionally rejected for alleged obviousness-type double patenting over claims 1-6, 12, 17, 21, 22, 26-28 and 34 of copending Application No. 10/518,732, over claims 1-13 of copending Application No. 10/547,654, and over claims 1-17 over copending Application No. 10/548,057. Claims 1-8 and 16-18 have been provisionally rejected for alleged obviousness-type double patenting over claims 14, 17, 18, 21, 22, 33, 34, 36-39 and 41 of copending Application No. 11/441,201.

The double patenting rejections are respectfully traversed. Claim 1, which is the sole independent claim, has been amended to incorporate the limitations of original claim 20. The Office has found claim 20 to be free of double patenting. Accordingly applicants respectfully submit that all of the double patenting rejections have been overcome.

CONCLUSION

In view of the amendments and the preceding remarks applicants submit that this application is now in condition for allowance. Applicants respectfully request reconsideration and withdrawal of all objections and rejections.

It is believed that no fee, other than the extension of time fee, is required in connection with the filing of this Amendment. If any additional fee is required, the Commissioner is hereby authorized to charge the amount of such fee to Deposit Account No. 50-1677.

Respectfully submitted,

/Lewis J. Kreisler/

Lewis J. Kreisler
Reg. No. 38522
Attorney for Applicant(s)

930 Clopper Road
Gaithersburg, MD 20878
Phone: (240) 631-2500 x3276
Facsimile: (240) 683-3794